

REMARKS**The Pending Claims:**

Claims 1-29, 31, 32, 34, 36, and 38-44 are pending. Claims 1-29, 31, 32, 34, 36 and 44 are under active consideration. Claims 38-43 are withdrawn from consideration. Claims 30, 33, 35 and 37 are canceled.

The Office Action:

Claims 1-38 and 44 are rejected.

Claim 30 is objected to.

The Amendment:

Claims 1, 34, 36, and 38 are currently amended. Claim 1 has been amended to include the limitations of claims 33 and 35. Claims 34, 36 and 38 have been amended to depend from claim 1, instead of canceled claim 33. The amendments are fully supported by the application as filed and do not add new matter.

Amendment of the claims is made without prejudice, without intent to abandon any originally claimed subject matter, and without intent to acquiesce in any rejection of record. Applicant expressly reserves the right to file one or more continuing applications hereof containing the canceled or unamended claims. Entry of the claim amendments is respectfully requested.

Summary of Examiner Interview:

A telephone interview was conducted on November 6, 2006. Participating in the interview were Examiner Robert Crow and Examiner Juliet Switzer of the United States Patent and Trademark Office, and Applicant's representative, Joel Silver. Discussed during the interview were the rejections to claims 1, 12, 33 and 35.

Applicants proposed incorporating the limitations of claims 35 and/or 12 into claim 1 to overcome the outstanding rejections. Particularly, Applicants asserted that in view of the proposed amendment there was no motivation to combine the cited references (Mirkin, Pinkel and Weiss), which would effectively render Mirkin inoperable for its

cited purpose. The Examiner suggested that Applicants submit a written response, which has been done in the following section of this paper.

Applicants would like to sincerely thank Examiner Crow and Switzer for their time and efforts in discussing the issues presented in the Official Action.

RESPONSE TO REJECTIONS**Rejection under 35 U.S.C. § 112, Second Paragraph:**

Claim 30 is rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Additionally, claim 30 is objected to for the alleged use of informalities. In view of the current amendment canceling claim 30, Applicants respectfully submit that the rejection has been rendered moot.

Rejection under 35 U.S.C. § 102(b):

Claims 1-5, 14-15, 17, 19, 24-25, 28, 30-32 and 44 are rejected under 35 U.S.C. § 102(b) as being anticipated by Mirkin et al. (WO 98/04740). Claims 33 and 35 are not rejected under 35 U.S.C. § 102(b). In view of the current amendment which incorporates the limitations of claims 33 and 35 into claim 1, applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 102(b).

Rejection under 35 U.S.C. § 103(a):

Claims 1, 33-34, and 36 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Mirkin in view of Pinkel (U.S. Patent No. 5,690,894). Additionally, claim 35 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Mirkin and Pinkel as applied to claim 33, and further in view of Weiss et al. (U.S. Patent No. 5,990,479). Although claims 33 and 35 are canceled by this amendment, the limitations therein are now included in claim 1. Accordingly, applicants address the rejections with respect to current claim 1.

According to the Office Action, “Mirkin et al does not teach separate determination of each binding event. However Pinkel et al teach a method of assaying samples for probes (e.g., using a biosensor array to detect nucleic acid binding complexes, Abstract) wherein each binding event is separately determined (e.g., simultaneous assaying of binding components of a test sample are done on by discretely detection at individual locations [i.e., bundles of fibers]; Abstract) with the added benefit

that the discrete addressing assists in rapid sample identification (Abstract). It would therefore have been obvious... to have modified the method comprising the detection as taught by Mirkin et al with separately determined detection as taught by Pinkel et al with reasonable expectation of success." Applicants respectfully disagree.

As recognized by the Office Action, Mirkin fails to describe a multiplex-type assay wherein multiple bidding events are separately detectable. This omission is not simply an oversight by Mirkin; instead, it represents a fundamental difference between Mirkin's disclosure and the present claims.

Mirkin describes a nucleotide detection assay that relies on a detectable change "brought about as a result of the hybridization of oligonucleotides on the nanoparticles to the nucleic acid." *Abstract*. The detectable change as a result of nucleotide hybridization is axiomatic to Mirkin. Where fluorescent dyes are described, there is a donor-acceptor motif, wherein dye quenching ceases upon hybridization to the target sequence.

The present rejection is based on the amplification scheme described in Figure 13, which involves aggregation of gold nanoparticles through hybridizable binding sequences, forming a dendritic-like matrix which manifests itself as a "darkened area" on the substrate (see Example 6). The purpose of this scheme, as with all other schemes in Mirkin, is to induce a detectable change in the mixture upon hybridization of the nucleotide sequences (page 74). Mirkin does not describe the use varying nanoparticles and tag sequences in Figure 13, because that is contrary to the primary objective, which is to amplify a signal. The sequences simply provide a facet for such amplification.

Conversely, the tag sequences in the present claims are designed for selective binding of distinct nanocrystals, thereby permitting multiplexing. Accordingly, Mirkin and the present claims are at cross purposes, such that a modification of either would render the other inoperable for its designed purpose.

According to the M.P.E.P. § 2143.01(VI) "If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious." *Citing, In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959). Furthermore, "The mere fact that references can be combined or modified does

not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). The desirability of the Office Action's proposed modification is not recognized in the prior and is contrary to the purpose of Mirkin.

Accordingly, it would not have been obvious to combine multiplexing described in Weiss and Pinkel to the methods described in Mirkin. The only basis on which that argument can be founded involves hindsight reconstruction of the present claims.

In view of the foregoing Applicants respectfully request withdrawal of the current rejections over Mirkin in view of Weiss and Pinkel.

The interview summary points out that sandwich assays are well known and that other art teaching the proposed method with labels other than nanocrystals may exist and that there would be a strong motivation to use nanocrystals with those methods. In view of this suggestion, Applicants have not added any additional limitations or material to the original claims as filed, which have been examined. Accordingly, no additional rejections are believed to be necessitated by this amendment and all of the previous rejections have been addressed.

CONCLUSION

In view of the above remarks, it is submitted that this application is now ready for allowance. Early notice to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned agent at (541) 335-0165.

Respectfully submitted,

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